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EDITORIAL COMMENT

Bare-Metal Versus Drug-Eluting Stent Placement Among Patients Presenting With Anemia*

Sharat Koul, DO, David J. Moliterno, MD

Lexington, Kentucky

Multiple studies among patients with acute coronary syndromes (ACS) and those undergoing percutaneous coronary intervention (PCI) have shown that anemia is a strong predictor for both short- and long-term adverse outcomes (1,2). In a large meta-analysis by Sabatine et al. (2) the presence of anemia was predictive for adverse events across the spectrum of ACS. For patients with ST-segment elevation myocardial infarction, when those with hemoglobin (Hb) values of 14 to 15 g/dl were used as the comparator, 30-day cardiovascular mortality increased as Hb levels

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fell below 14 g/dl, with an adjusted odds ratio (OR) of 1.21 (95% confidence interval [CI]: 1.12 to 1.30; $p < 0.001$) for each 1 g/dl decrement in Hb. Similarly, among those with non–ST-segment elevation ACS, using patients with Hb levels of 15 to 16 g/dl as the reference, the likelihood of cardiovascular death, subsequent myocardial infarction, or recurrent ischemia increased as the Hb fell below 11 g/dl, with an adjusted OR of 1.45 (95% CI: 1.33 to 1.58; $p < 0.001$) for each 1 g/dl decrement in Hb. Considering PCI patients, Lee et al. (1) observed a lower 1-year survival among 6,116 patients with anemia compared with those without (adjusted hazard ratio [HR] for Hb 10 to 12 g/dl: 1.5, 95% CI: 1.3 to 1.8, and for Hb <10 g/dl, 1.8, 95% CI: 1.3 to 2.3; $p = 0.004$).

Beyond anemia being associated with a worse cardiovascular prognosis, there are additional caveats and limitations in caring for such patients. For example, patients with baseline anemia are known to be at increased risk for ACS- and PCI-related bleeding events. Manoukian et al. (3) found anemia to be a strong independent predictor for major bleeding (OR: 1.87, 95% CI: 1.54 to 2.28; $p < 0.0001$) in the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) study, which assessed bivalirudin versus heparin with platelet IIb/IIIa inhibitors among 13,819 ACS-PCI patients. This and other recent studies (3,4) have also emphasized the relationship between bleeding and subsequent mortality. In the ACUITY study, 30-day mortality was 7.3% versus 1.2% among patients with and without bleeding, respectively (OR: 7.55, 95% CI: 4.68 to 12.18; $p < 0.0001$). Therefore, as polypharmacy anticoagulation strategies continue to emerge, it can be expected that bleeding will remain a pressing and persistent risk among ACS and PCI patients, particularly as the age of the general population and related comorbidities (e.g., atrial fibrillation) increase (5).

For PCI patients, concerns regarding bleeding continue beyond the catheterization laboratory and the index hospitalization because an ischemia-reduction benefit from long-term dual antiplatelet therapy is established for ACS treatment and separately for drug-eluting stents (DES). A meta-analysis by Serebruany et al. (6) studied the bleeding risks associated with dual-agent versus single-agent therapy and found that dual antiplatelet therapy was associated with an increased relative risk of major (relative risk [RR]: 1.47, 95% CI: 1.36 to 1.60) and minor bleeding events (RR: 1.56, 95% CI: 1.47 to 1.66). Putting these multiple anemia- and bleeding-related issues together, and synergized by concerns for stent thrombosis, it is understandable why there is pause on the part of interventional cardiologists when selecting drug-eluting versus bare-metal stents among patients presenting with anemia.

The paper by Shishehbor et al. (7) in this issue of *JACC: Cardiovascular Interventions* provides some helpful insight and cause for further reflection. In this first large-scale retrospective study to specifically address the use of DES versus bare-metal stents among anemic patients, the investigators suggest that DES may be used safely in this patient group. Considering a multiyear interval with more than 11,000 PCI patients, 2,172 or roughly 20%, were found to have baseline anemia (as defined by World Health Organization). All-cause mortality at a 1.8-year median follow-up was significantly lower for those treated with DES in unadjusted and multivariable-adjusted Cox proportional models (HR: 0.66, 95% CI: 0.54 to 0.82; $p < 0.001$). Considering anemia cut points according to hematocrit levels of ≤28%, 29% to 35%, and ≥35%, Shishehbor et al. (7) observed mortality to be inversely proportional at approximately 35%, 25%, and 15%, respectively. For each of these hematocrit cut points, mortality was lower for patients receiving DES.

A concept that may be hypothesized from this manuscript is that the heightened mortality risk associated with anemia may necessitate a more effectual form of PCI treatment. Whether any mortality benefit is from the antirestenotic

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From the Gill Heart Institute and Division of Cardiovascular Medicine, University of Kentucky, Lexington, Kentucky. Dr. Moliterno has received past honoraria for serving as a member of data safety monitoring committees for stent manufacturers including Boston Scientific and Guidant.

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effects of DES, the associated dual-antiplatelet therapy, or undefined factors is uncertain. Because numerous studies have shown that DES are particularly beneficial in higher risk populations—patients with diabetes, end-stage renal disease, and complicated coronary artery disease—it might be plausible that DES provide a net mortality benefit to those with anemia despite increased bleeding risks. As new, more powerful antiplatelet agents such as prasugrel, cangrelor, and ticagrelor (8,9) and newer generation DES are developed, this hypothesis should be considered. Regardless, prospective studies will be needed that collect important information unavailable in the Shishehbor et al. (7) dataset such as bleeding events, stent thrombosis, duration of dual antiplatelet therapy, and other factors associated with the selection of bare-metal stents versus DES in current practice.

Reprint requests and correspondence: Dr. David J. Moliterno, Department of Cardiovascular Medicine, University of Kentucky, 900 South Limestone Avenue, 317 Wethington Building, Lexington, Kentucky 40536-0200. E-mail: Moliterno@uky.edu.

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Key Words: acute coronary syndromes ■ anemia ■ bare-metal stents ■ drug-eluting stents ■ hemoglobin ■ percutaneous coronary intervention.